REMARKS

Claims 1-3, 8, 9 and 28 will remain pending.

Obviousness-Type Double Patenting

Claims 1-3, 8-9 and 28 are rejected on the grounds of nonstatutory obviousness-type double patenting as being allegedly unpatentable over claims 1-11 of U.S. 7,524,628; over claims 1-16 of U.S. 7,045,286 in view of U.S. 5,922,553; over claims 1-2, 4-6, 8-12, 14-16, 18-24 of U.S. 7,361,464; and over claims 1-3, 5-7, 9, 11-14, 16-18, 20, 22-24 of U.S. 7,341,831. Without conceding the propriety of these rejections, terminal disclaimers over each of the foregoing prior patents are filed herewith to overcome these rejections.

Rejection under 35 U.S.C. §112, first paragraph (written description)

Claims 1-3, 8-9 and 28 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. Examiner alleges that the newly added limitation "that is not labeled with a radioactive label or a fluorescent label" does not have support in the specification. However, the specification at page 16, ln. 24 states that "[i]n one embodiment, the nucleic acid sequence is detectably labeled such as with a radioactive label or a fluorescent label. In a preferred embodiment, the nucleic acid sequence is *not labeled but rather is stained* by fluorescent dye." (emphasis added) Applicants respectfully submit that this passage provides support for the newly added limitation and respectfully request removal of the rejection.

Rejection under 35 U.S.C. §103(a) (obviousness)

Claims 1-3, 8-9 and 28 have been rejected under 35 U.S.C. §103(a) as being allegedly unpatentable over Eberwine (5,922,553) in view of Eberwine (7,115,371), Waggoner (5,627,027) and Sano (5,665,539). As discussed in the previous reply, applicants agree with the examiner that Eberwine '553 does not disclose a monoclonal antibody which binds to a selected epitope comprising a universal epitope. Eberwine '371 discloses a single chain Fv or CDR which contains a universal epitope, but it does not teach or suggest the use of biotin-

streptavidin linkers to bind the Fv or CDR to the oligonucleotide. Sano discloses the use of a biotin-streptavidin linker to attach marker DNA to antibody. However, Sano does not teach or suggest the use of a monoclonal antibody which binds to a selected epitope comprising a universal epitope.

Eberwine and Sano fail to teach the linear quantification of the molecule comprising the selected epitope by staining the RNA amplification product with a fluorescent dye. Further addition of the teaching in Waggoner does not cure the gaps in Eberwine and Sano.

The examiner alleges in the present office action that Waggoner discloses that cyanine dye can be used to attach to fragments of DNA or RNA to identify the presence and quantity of a specific nucleotide sequence in samples of DNA or RNA, and that the attachment of cyanine dye to DNA or RNA fragments is interpreted as fluorescent dye staining a DNA or RNA fragment. (citing col. 8, ln. 51-56) As discussed in our previous reply, the passage cited in Waggoner states that "luminescent cyanine and related dyes can be attached to fragments of DNA or RNA. The labeled fragments of DNA or RNA can be used as fluorescent hybridization *probes* to identify the presence and quantity of specific complementary nucleotide sequences in samples of DNA or RNA." Therefore, Waggoner discloses the use of cyanine-*labeled RNA probes* for hybridization to a target sequence, and not the staining of *unlabeled* amplified RNA with cyanine dye. In fact, Waggoner states at column 4, lines 35-45 that "[t]his invention relates to the *covalent* reaction of highly luminescent and highly light absorbing cyanine…" (emphasis added). Waggoner also states at column 9, lines 21-27 that "[t]he present invention pertains to methods for *covalently* attaching luminescent cyanine and cyanine-type dyes to biological materials…" (emphasis added). The use of cyanine dyes as a *stain*, as in our invention, does not involve *covalent* attachment of cyanine dyes, but rather the intercalation of the dye in the nucleic acid. (See Example 1 at page 26 in Application which refers to the use of "intercalating dye RiboGreen", which is a cyanine intercalating agent). Waggoner also states at column 7, lines 61-65 that "[t]his invention *requires* cyanine dyes to be modified by the incorporation into the cyanine molecule of a reactive group that will *covalently* attach to a target molecule." (emphasis added) Thus, Waggoner *requires* the covalent attachment of cyanine dyes to the target molecule, and therefore the examiner's interpretation of Waggoner referring to staining of DNA or RNA is mistaken.

These facts, taken together with the other art cited by the Examiner as discussed supra, fail to support a *prima facie* case of obviousness.

Applicants respectfully submit that the present application is in condition for allowance. Favorable consideration and an early notice of allowance are respectfully requested.

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